

LECTURE NOTES ON: FREE-ENERGY CALCULATIONS

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Abstract

Techniques to compute absolute free energies of classical many-body systems are discussed with special emphasis on those techniques that can be used to map the phase diagram of solids and liquids. Recent technical advances in the study of multi-component systems and systems consisting of flexible molecules are emphasized.

1 Introduction

These lectures describe a number of techniques that have been developed to evaluate the free energy of classical many-body systems. However, before I start discussing old and new tricks to compute free energies, I should first explain *why* there is much interest in such techniques. Asking this question is not as strange as it may seem, because one is only rarely interested in free energy *for its own sake*. In this respect, free energy calculations are very different from, say, a simulation study of the structure of a liquid-vapor interface. In the latter case, all quantities of physical interest (e.g. the surface tension or the density profile) can be directly measured during the simulation. In contrast, the information obtained in a free-energy calculation is almost always used to compute something else that is of physical interest, e.g. the location of a phase transition, the solubility of one compound in another or the concentration of point defects in a crystalline solid. As we shall see later, it is sometimes possible to compute phase equilibria *directly*, i.e. without first computing the free energy. Under such circumstances only a masochist would still compute the free energy. This example illustrates our curious love-hate relation with free energy calculations: we often need them, but we wish that we could live without them.

There is another unusual feature that distinguishes a numerical calculation of the free energy from, say, a measurement of the equation-of-state of a liquid. Namely that we *can* measure the pressure (or density) of a fluid in a simulation, but we *cannot* measure the free energy. The reason is simple: the Helmholtz free energy F is related to the canonical partition function of a many-body system through

$$F = -k_B T \ln Q(N, V, T), \quad (1)$$

where T is the absolute temperature, k_B is Boltzmann's constant and $Q(N, V, T)$ is the canonical partition function of a system of N particles in volume V at temperature T . For a classical many-body system, $Q(N, V, T)$ is of the form

$$Q(N, V, T) = \frac{q^N(T)}{N!} \int d\mathbf{q}^N \exp(-\beta U(\mathbf{q}^N)). \quad (2)$$

In eq. 2, \mathbf{q}^N designate the coordinates (translational or other) of all N particles, $q(T)$ denotes the 'kinetic' contribution to the partition function that results from integration over the momenta conjugate to \mathbf{q}^N (e.g. for atomic systems, $q(T) = (2\pi m k_B T / h^2)^{3/2}$) and $U(\mathbf{q}^N)$ is the potential energy function of this N -particle system. Although Molecular Dynamics or Monte Carlo simulations can be used to measure averages of the type

$$\langle A \rangle \equiv \frac{q^N(T)}{N!} \frac{\int d\mathbf{q}^N A(\mathbf{q}^N) \exp(-\beta U(\mathbf{q}^N))}{Q(N, V, T)}, \quad (3)$$

neither technique can measure $Q(N, V, T)$ (and hence F) directly. This implies that a numerical 'measurement' of the free energy must be rather different from a measurement of, say, the compressibility. The practical consequence of the special problems associated with the numerical measurement of a 'thermal' quantity, such as the free energy (or the entropy S or the Gibbs free energy G), is that special techniques are required to perform such measurements. In fact, as we shall see below, almost all calculations that are referred to as 'free-energy calculations' do not actually measure an absolute free energy at all, but rather the *difference* between two free energies.

In summary: free energies are usually not computed for their own sake, but because they allow us to determine phase or chemical equilibria. 'Thermal' quantities, such as the Helmholtz free energy are related to the volume of the accessible configuration space, rather than to an average over this space. Therefore, special techniques are required to compute free energies.

Thus far this introduction may not have sounded as an advertisement for free-energy calculations. Now, however, I will not restrain myself anymore and admit that many of the techniques to compute free energies are both elegant and instructive. I, for one, have learned more from computer 'experiments' about the meaning of, for example, the chemical potential than from any textbook on statistical mechanics or thermodynamics.

The material presented in these lectures is organised as follows. I start with a brief introduction to numerical techniques to locate phase equilibria. In particular, I shall explain what role free energy calculations play in such computer studies. Next, I present a brief description of the 'Widom' method to measure the chemical potential of atomic or simple molecular fluids (section 3.1). I then show how this technique can be extended to deal with flexible molecules. Subsequently, I discuss three general schemes to measure free-energy differences, namely the overlapping distribution method, the acceptance ratio method and the method of 'umbrella sampling'. Finally I consider simulation schemes that allow us to study phase coexistence *without* the need to compute the free energy of all coexisting phases. In all cases, I try to include references to recent work although I should warn the reader that this is not a review nor a bibliography: a comprehensive discussion of the vast literature on this subject falls outside the scope of the present 'tutorial' paper.

2 Phase transitions

The study of phase transitions by computer simulation has grown to become a subject in its own right to which entire books are devoted (see e.g. [1]). The reason is not so much that unconventional methods of computer simulation are involved in such studies, but rather that a numerical study of the precise location and character of a phase transition often requires a lot subtle analysis. In other words, it is not only a matter of *how* to compute but *what*. Actually there is quite a difference between the tools used to study first-order phase transitions and those applied to analyse critical phenomena near continuous phase transitions. As these lectures are about free-energy calculations, I shall only discuss first-order phase transitions. The reason is that, at a higher-order phase transition, the free energy is continuous and hence free energy calculations are of no use in locating the transition point. For a discussion of techniques to analyse continuous phase transitions, I refer the reader to the relevant literature (e.g. refs. [2] and [1]).

2.1 First order phase transitions

In section 1 it was mentioned that knowledge of ‘thermal’ quantities, such as μ , is usually necessary to locate the coexistence line for a first-order phase-transition. At first sight knowledge of μ may appear superfluous. After all, a computer simulation mimics the behaviour of a real solid or liquid. If the simulation is ergodic it should spontaneously transform to whatever phase is thermodynamically most stable, and then we would know all there is to know. Unfortunately, this approach does not work. At least, not for phase transitions involving three-dimensional solids. At a solid-solid or solid-liquid phase transition very strong hysteresis effects are usually observed in a simulation (see figure 1). In



Figure 1: First-order phase transitions in small model systems with periodic boundary conditions (right) tend to exhibit much stronger hysteresis effects than are usually observed in the real world (left)

fact, it is very difficult to nucleate a crystal from a liquid during a simulation. Hence, to locate the point where two phases coexist, we must compute the chemical potential of the homogeneous phases at the same temperature and pressure and find the point where the two μ 's are equal. In the following sections, I discuss methods to compute μ and related thermal quantities by computer simulation (see also ref. [16]). In the present section I wish

to describe a simple, and usually reliable, method to compute the free energy F (and hence μ).

Let us first recall how free energies are measured in real experiments. In the real world free energies cannot be obtained from a single measurement either. What can be measured, however, is the derivative of the free energy with respect to volume V and temperature T :

$$\left(\frac{\partial F}{\partial V}\right)_{NT} = -P \quad (4)$$

and

$$\left(\frac{\partial F/T}{\partial 1/T}\right)_{VT} = E. \quad (5)$$

Here P is the pressure and E the energy of the system under consideration. The trick is now to find a reversible path that links the state under consideration to a state of known free energy. The change in F along that path can then simply be evaluated by integration of eqs. 4 and 5. There are only very few thermodynamic states where the free energy of a substance is known. One state is the ideal gas phase, the other is the perfectly ordered ground state at $T = 0K$.

In computer simulations, the situation is quite similar. In order to compute the free energy of a dense liquid, one may construct a reversible path to the very dilute gas phase. It is not really necessary to go all the way to the ideal gas. But at least one should reach a state that is sufficiently dilute that the free energy can be computed accurately, either from knowledge of the first few terms in the virial expansion of the compressibility factor $PV/(NkT)$, or that the chemical potential can be computed by other means (see section 3.1 and 3.3 below). For the solid, the ideal gas reference state is less useful (although techniques have been developed to construct a reversible path from a dense solid to a dilute (lattice) gas [3]). The obvious reference state for solids is the harmonic lattice. Computing the absolute free energy of a harmonic solid is relatively straightforward, at least for atomic and simple molecular solids. However, not all solid phases can be reached by a reversible route from a harmonic reference state. For instance, in molecular systems it is quite common to find a strongly anharmonic plastic phase just below the melting line. This plastic phase is not (meta-) stable at low temperatures.

Fortunately, in computer simulations we do not have to rely on the presence of a ‘natural’ reversible path between the phase under study and a reference state of known free energy. If such a path does not exist, we can construct an artificial path. This is in fact a standard trick in statistical mechanics (see e.g. [4]). It works as follows: Consider a case where we need to know the free energy $F(V, T)$ of a system with a potential energy function U_1 , where U_1 is such that no ‘natural’ reversible path exists to a state of known free energy. Suppose now that we can find another model system with a potential energy function U_0 for which the free energy *can* be computed exactly. Now let us define a generalized potential energy function $U(\lambda)$, such that $U(\lambda = 0) = U_0$ and $U(\lambda = 1) = U_1$. The free energy of a system with this generalized potential is denoted by $F(\lambda)$. Although $F(\lambda)$ itself cannot be measured directly in a simulation, we can measure its derivative with respect to λ :

$$\left(\frac{\partial F}{\partial \lambda}\right)_{NVT\lambda} = \left\langle \frac{\partial U(\lambda)}{\partial \lambda} \right\rangle_{NVT\lambda} \quad (6)$$

If the path from $\lambda = 0$ to $\lambda = 1$ is reversible, we can use eq. 6 to compute the desired $F(V, T)$. We simply measure $\langle \partial U / \partial \lambda \rangle$ for a number of values of λ between 0 and 1. Typically, 10 quadrature points will be sufficient to get the absolute free energy per particle accurate to within $0.01 k_B T$. It is however important to select a reasonable reference system. One of the safest approaches appears to be to choose as a reference system an Einstein crystal with the same structure as the phase under study [5]. This choice of reference system makes it extremely improbable that the path connecting $\lambda = 0$ and $\lambda = 1$ will cross an (irreversible) first order phase transition from the initial structure to another, only to go back to its original structure for still larger values of λ . Nevertheless, it is important that the parametrization of $U(\lambda)$ be chosen carefully. Usually, a linear parametrization (i.e. $U(\lambda) = \lambda U_1 + (1 - \lambda)U_0$) is quite satisfactory. But occasionally such a parametrization may lead to weak (and relatively harmless) singularities in eq. 6 for $\lambda \rightarrow 0$. More details about such free energy computations can be found in ref. [16].

Similar techniques can be used to locate first-order phase transitions involving phases with partial order (e.g. liquid crystals). For details, the reader is referred to refs [6, 7, 8]. The first numerical determination of the melting point of a molecular crystal was recently published by Meijer et al. [9]. Finally, thermodynamic integration techniques are particularly useful to compute the Gibbs free energy of mixtures. A recent application is the work of Kranendonk and Frenkel, who have computed the melting curve of a substitutionally disordered solid mixture of hard spheres with different size [10]. In this case, thermodynamic integration is used to slowly change the size-ratio of the particles at fixed volume fraction. The reference point is size ratio $\alpha = 1$ ('isotopic mixture'). The reversible work needed to change the size ratio from 1 to a given value of α is a direct measure for the excess free energy of the solid solution at that composition. For details, the reader is referred to ref. [11].

3 Techniques to measure the chemical potential

3.1 Particle insertion method

A particularly simple and elegant method to measure the chemical potential μ of a species in a pure fluid or in a mixture is the 'particle-insertion' method (often referred to as the Widom-method [12]). The statistical mechanics that is the basis for this method is quite simple. Consider the definition of the chemical potential μ_α of a species α . From thermodynamics we know that μ is defined as:

$$\begin{aligned} \mu &= \left(\frac{\partial G}{\partial N} \right)_{PT} \\ &= \left(\frac{\partial F}{\partial N} \right)_{VT} \\ &= -T \left(\frac{\partial S}{\partial N} \right)_{VE} \end{aligned} \quad (7)$$

Where G , F and S are the Gibbs free energy, the Helmholtz free energy and the entropy, respectively. Here, and in the next few paragraphs we focus on a one-component system, and hence we drop the subscript α . Let us first consider the situation at constant NVT .

If we express the Helmholtz free energy of an N -particle system in terms of the partition function Q_N (eq. 50), then it is obvious from eq. 7 that, for sufficiently large N the chemical potential is given by: $\mu = -kT \ln(Q_{N+1}/Q_N)$. If we use the explicit form (eq. 50) for Q_N , we find:

$$\begin{aligned} \mu &= -kT \ln(Q_{N+1}/Q_N) \\ &= -kT \ln\left(\frac{qV}{(N+1)}\right) - kT \ln\left(\frac{\int ds^{N+1} \exp(-\beta U(\mathbf{s}^{N+1}))}{\int ds^N \exp(-\beta U(\mathbf{s}^N))}\right) \\ &= \mu_{id}(V) + \mu_{ex} . \end{aligned} \tag{8}$$

In the first line of eq. 8, we have assumed that the system is contained in a cubic box with diameter $L = V^{1/3}$ and have defined scaled coordinates \mathbf{s}^N , by:

$$\mathbf{q}_i = L\mathbf{s}_i$$

for $i = 1, 2, \dots, N$. In the last line of eq. 8, we have indicated the separation in the ideal-gas contribution to the chemical potential, and the excess part. As $\mu_{id}(V)$ can be evaluated analytically, we focus on μ_{ex} . We now separate the potential energy of the $N+1$ -particle system into the potential energy function of the N -particle system, $U(\mathbf{s}^N)$, and the interaction energy of the $N+1$ -th particle with the rest: $\Delta U \equiv U(\mathbf{s}^{N+1}) - U(\mathbf{s}^N)$. Using this separation, we can write μ_{ex} as:

$$\mu_{ex} = -kT \ln \left\langle \int ds_{N+1} \exp(-\beta \Delta U) \right\rangle_N , \tag{9}$$

where $\langle \dots \rangle_N$ denotes canonical ensemble averaging over the configuration space of the N -particle system. The important point to note is that equation 9 expresses μ_{ex} as an ensemble average that can be sampled by the conventional Metropolis scheme. There is only one aspect of this equation that makes it different from the averages that we considered before, namely the fact that we compute the average of an *integral* over the position of particle $N+1$. This last integral can be sampled by brute-force (unweighted) Monte Carlo sampling. In practice the procedure is as follows: we carry out a perfectly normal constant NVT Monte Carlo simulation on the system of N particles. At frequent intervals during this simulation (for instance, after every MC trial move) we randomly generate a coordinate \mathbf{s}_{N+1} , uniformly over the unit cube. With this value of \mathbf{s}_{N+1} , we then compute $\exp(-\beta \Delta U)$. By averaging the latter quantity over all generated trial positions, we obtain the average that appears in eq. 9. So, in effect, we are computing the average of the Boltzmann factor associated with the random insertion of an additional particle in an N -particle system, *but we never accept any such trial insertions*, because then we would no longer be sampling the average needed in eq. 9. The Widom method is a very powerful method to compute the chemical potential of (not too dense) atomic and simple molecular liquids. Its main advantage is its great simplicity, and the fact that it can be added on to an existing constant- NVT MC program, without any modifications to the original sampling scheme: we are simply computing one more thermal average. There is something else about the Widom method that makes it appealing, but that has nothing to do with computational efficiency: it really provides an insight into the *meaning* of the chemical potential. An insight that is often hard to extract from most text-books on statistical thermodynamics.

The extension of the Widom method to other ensembles, in particular NPT and NVE is relatively straightforward. However, it would be incorrect simply to apply equation 9 to these other ensembles. As this point is not always fully appreciated in the literature, I shall briefly discuss the application of the Widom method to the NPT -ensemble (see refs. [13, 15]) and to the NVE -ensemble (see ref. [16]). To derive the expression for the chemical potential in the NPT -ensemble, we start from eq. 54:

$$G(N, P, T) = -kT \ln \int dV \frac{(qV)^N \exp(-\beta PV)}{N!} \int ds^N \exp(-\beta U(s^N; V)).$$

We must evaluate $\mu = (\partial G / \partial N)_{PT}$. Entirely analogously to the NVT case we find that $\mu = G(N + 1, P, T) - G(N, P, T)$ equals:

$$\begin{aligned} \mu &= -kT \ln \left\langle \frac{qV}{(N+1)} \int ds_{N+1} \exp(-\beta \Delta U) \right\rangle \\ &= -kT \ln(qkT/P) - kT \ln \left\langle \frac{PV}{(N+1)kT} \int ds_{N+1} \exp(-\beta \Delta U) \right\rangle \\ &= \mu_{id}(P) + \mu_{ex}(P) \end{aligned} \quad (10)$$

Two points should be noted: first of all we now define the ideal gas reference state at the same pressure, rather than at the same average density as the system under study. And secondly, the fluctuating quantity that we are averaging is no longer $\exp(-\beta \Delta U)$, but $V \exp(-\beta \Delta U)$. In practice, one should only expect the fluctuating volume term in eq. 10 to be important if large volume fluctuations are possible, for instance in the vicinity of phase transitions. But chemical potentials are often calculated precisely to locate such phase transitions.

In the constant- NVE ensemble, i.e. the one probed by conventional Molecular Dynamics simulations, we start from the relation: $\mu/T = -(\partial S / \partial N)_{VE}$. In the microcanonical ensemble, the entropy S is related to $\Omega(N, V, E)$, the total number of accessible states, by the famous relation $S = k \ln \Omega(N, V, E)$. The classical expression for $\Omega(N, V, E)$ is:

$$\Omega(N, V, E) = \frac{1}{h^{3N} N!} \int \delta(H(\mathbf{p}^N, \mathbf{q}^N) - E) d\mathbf{p}^N d\mathbf{q}^N. \quad (11)$$

Again the derivation proceeds much as before, but for the fact that we must now compute $\Omega(N + 1, V, E) / \Omega(N, V, E)$. This is slightly more cumbersome (see [16]) and we only quote the final result:

$$\beta \mu_{ex} = -\ln \{ \langle T \rangle^{-3/2} \langle T^{3/2} \exp(-\Delta U / kT) \rangle \}, \quad (12)$$

where T is the (fluctuating) temperature (as determined from the instantaneous kinetic energy of the particles). Such fluctuations tend to be large where the heat capacity of the system is large (see ref. [17]).

The particle insertion method can be modified to measure the *difference* in chemical potential between two species α and β in a mixture. In this case a trial move consists of an attempt to transform a particle of species α into species β (without, of course, ever accepting such trial moves). This topic is briefly discussed in section 4.4. For more details, the reader is referred to refs. [14, 15]. Let me finally mention that the particle insertion and swapping techniques are not limited to the measurement of chemical potentials. In fact, a

wide class of partial molar quantities (such as, for example the partial molar enthalpy h_α or the partial molar volume v_α) can be measured in this way. For details, see refs. [15, 18]

The particle insertion method fails when the probability of ‘accepting’ a trial insertion becomes very small. One consequence is that the simple particle insertion method is less suited for molecular than for atomic systems (see figure 2). However, quite recently, Siep-



Figure 2: The particle insertion method is less efficient for ‘molecular’ systems (right), than for ‘atomic’ systems (left)

mann [19] has developed a scheme to measure the chemical potential of flexible molecules with a finite number of conformations. The next section discusses the basic idea behind this scheme.

3.2 Chemical potential of flexible molecules

In order to understand the recent developments in the calculation of the chemical potential of chain molecules, it is instructive to first consider how we would compute μ_{ex} of a chain molecule with the Widom technique. To this end, I introduce the following notation: the position of the first segment of the chain molecule is denoted by \mathbf{q} and the conformation of the molecule is described by Γ . The configurational part of the partition function of a system of chain molecules can be written as

$$Q_{chain}(N, V, T) = \frac{1}{N!} \int d\mathbf{q} \sum_{\Gamma_1, \dots, \Gamma_n} \exp(-\beta U(\mathbf{q}^N, \Gamma^N)). \quad (13)$$

The analogy with the previous sections suggests that the excess chemical potential of a chain molecule is obtained by considering the ratio

$$Q(N+1, V, T) / [Q(N, V, T)Q_{non-interacting}(1, V, T)],$$

where of the $Q(N+1, V, T)$ is the (configurational part of) the partition function of a system of $N+1$ interacting chain molecules and $Q(N, V, T)Q_{non-interacting}(1, V, T)$ the partition function for a system consisting of N interacting chains and one chain that does not interact with the others. The latter chain plays the role of the ideal gas molecule in the previous sections. Note, however, that although this molecule does not interact with any of the other molecules it *does* interact with itself, both through bonded and through non-bonded

interactions. Unfortunately, this is not a particularly useful reference state, as we do not, in general, know the partition function of an isolated self-avoiding chain.

We therefore use another reference state, namely that of the isolated non-selfavoiding chain. To be specific, let us consider the case of a molecule that consists of ℓ segments. Starting from segment 1, we can add segment 2 in b_2 equivalent directions, and so on. Clearly, the total number of non-selfavoiding conformations is $\Omega_{id} = \prod_{i=1}^{\ell} b_i$. For convenience, I have assumed that for a given i , all b_i directions are equally likely (i.e. I ignore *gauche-trans* potential energy differences and I even allow the ideal chain to fold back on itself). These limitations are not essential but they simplify the notation. Finally, I assume that all b_i are the same. Hence, for the simple model that we consider, $\Omega_{id} = b^{\ell}$. If we use such an ideal chain as our reference system, the expression for the excess chemical potential becomes

$$\begin{aligned} \beta\mu_{ex} &= -k_B T \ln \left(\frac{Q_{chain}(N+1, V, T)}{Q(N, V, T)Q_{ideal}(1, V, T)} \right) \\ &= -k_B T \ln \langle \exp[-\beta\Delta U(\mathbf{q}^N, \Gamma^N; \mathbf{q}_{N+1}, \Gamma_{N+1})] \rangle, \end{aligned} \quad (14)$$

where ΔU denotes the interaction of the test chain with the N chains that are already present in the system *and with itself*, while $\langle \dots \rangle$ indicates averaging over all starting positions and all ideal-chain conformations of a randomly inserted chain.

The problem with the Widom approach to eq. 14 is that almost all randomly inserted ideal chain conformations will overlap either with particles already present in the system, or internally. The most important contributions to μ_{ex} will come from the extremely rare cases where the trial chain happens to be in just the right conformation to fit into the available space in the fluid. Clearly, it would be desirable if we could restrict our sampling to those conformations that satisfy this condition. If we do that, we introduce a bias in our computation of the insertion probability and we must somehow correct for that bias. The scheme developed by Siepmann shows how that can be done.

In order to explain this scheme, I will first describe how the method works, and then show that it does indeed lead to the desired answer. The approach used in ref. [19] consists of two steps: in the first step a chain conformation is generated in such a way that ‘acceptable’ conformations are created with a high probability. The next step corrects for this bias by multiplying with a weight factor. A scheme that generates ‘acceptable’ chain conformations with a high probability was developed by Rosenbluth and Rosenbluth in the early fifties [20]. In the Rosenbluth scheme, a conformation of a chain molecule is constructed segment-by-segment. For every segment, we have a choice of b possible directions. In the Rosenbluth scheme, this choice is not random but favors the direction with the largest Boltzmann factor. To be specific, the probability (P) to generate a polymer with a conformation Γ using the Rosenbluth algorithm is given by

$$P_{\Gamma} = \prod_{i=1}^{\ell} \frac{\exp[-\beta u_{\Gamma_i}]}{\sum_{j=1}^b \exp[-\beta u_{\Gamma_i}(j)]}, \quad (15)$$

where u_{Γ_i} denotes the energy of segment i of the chain with conformation Γ (note that this energy excludes the contributions of segments $i+1$ to ℓ , so the total energy of the chain is given by: $U_{\Gamma} = \sum_{i=1}^{\ell} u_{\Gamma_i}$), j enumerates all possible orientations from which the i -th

segment of the chain can be chosen. Finally, $u_{\Gamma_i}(j)$ denotes the potential energy of the i -th segment in orientation j . An important property of the probability given by eq. 15 is that it is normalized, i.e

$$\sum_{\Gamma} P_{\Gamma} = 1.$$

The Rosenbluth weight factor that corrects for the bias in the selection of conformation Γ is given by

$$W_{\Gamma} \equiv \prod_{i=1}^{\ell} \left[\frac{1}{b} \sum_{j=1}^b \exp[-\beta u_{\Gamma_i}(j)] \right]. \quad (16)$$

Now let us assume that we use the Rosenbluth scheme to generate a large number of chain conformations while keeping the coordinates of all other particles in the system fixed. For this set of conformations, we compute the average of the Rosenbluth weight factor W , \overline{W} . If we also perform an ensemble average over all coordinates and conformations of the N particles in the system, we obtain

$$\langle W \rangle = \left\langle \sum_{\Gamma} P_{\Gamma}(\mathbf{q}^N, \Gamma^N) W_{\Gamma}(\mathbf{q}^N, \Gamma^N) \right\rangle \quad (17)$$

where the angular brackets denote the ensemble average over all configurations of the system $\{\mathbf{q}^N, \Gamma^N\}$ of the 'solvent'. Note that the test polymer does not form part of the N -particle system. Therefore the probability to find the remaining particles in a configuration $\{\mathbf{q}^N, \Gamma^N\}$ does not depend on the conformation Γ of the polymer.

In order to simplify the expression for the average in eq. 17, we first consider the average of the Rosenbluth factor for a given configuration $\{\mathbf{q}^N, \Gamma^N\}$ of the solvent.

$$\overline{W}(\{\mathbf{q}^N, \Gamma^N\}) = \sum_{\Gamma} P_{\Gamma}(\mathbf{q}^N) W_{\Gamma}(\{\mathbf{q}^N, \Gamma^N\}), \quad (18)$$

Substitution of equations (15) and (16) yields

$$\begin{aligned} \overline{W} &= \sum_{\Gamma} \left[\prod_{i=1}^{\ell} \frac{\exp[-\beta u_{\Gamma_i}]}{\sum_{j=1}^b \exp[-\beta u_{\Gamma_i}(j)]} \right] \left[\prod_{i=1}^{\ell} \frac{1}{b} \sum_{j=1}^b \exp[-\beta u_{\Gamma_i}(j)] \right] \\ &= \sum_{\Gamma} \prod_{i=1}^{\ell} \frac{1}{b} \exp[-\beta u_{\Gamma_i}] \\ &= \sum_{\Gamma} \frac{1}{b^{\ell}} \exp[-\beta U_{\Gamma}], \end{aligned} \quad (19)$$

where we have dropped all explicit reference to the solvent coordinates $\{\mathbf{q}^N, \Gamma^N\}$. Note that eq. 19 can be interpreted as an average over all *ideal* chain conformations of the Boltzmann factor $\exp[-\beta U_{\Gamma}]$. If we now substitute eq. 19 in eq. 18 we obtain

$$\langle W \rangle = \frac{\sum_{\Gamma} \langle \exp[-\beta \Delta U(\mathbf{q}^N, \Gamma^N; \mathbf{q}_{N+1}, \Gamma_{N+1})] \rangle}{\sum_{\Gamma}} \quad (20)$$

If we compare eq. 20 with eq. 14, we see that the ensemble average of the Rosenbluth factor is directly related to the excess chemical potential of the chain molecule.

$$\beta\mu_{ex} == -k_B T \ln \langle W \rangle , \quad (21)$$

This completes our proof that the Siepmann's scheme to measure the average Rosenbluth factor of a trial chain can indeed be used to measure the excess chemical potential of a polymer in a dense fluid.

Siepmann has compared this method with a brute force application of the Widom method for a simple two-dimensional model of chain molecules on a lattice [19], and found the 'Rosenbluth' scheme to be very much superior, in particular at high densities. I should stress that the above method to measure the chemical potential is in no way limited to chain molecules on a lattice. What *is* essential is that the number of possible directions for each segment (b) relative to the previous one is finite. Recently, Kumar and Panagiotopoulos [21] have developed an approximate scheme to compute the chemical potential of a fully flexible chain molecule. Recent work by Frenkel and Smit [22] shows that it is even possible to construct a rigorous scheme to compute the chemical potential of fully (or partially) flexible molecules. The special case of chain molecules on a lattice was studied by Mooij and Frenkel [23, 24] who found that, in that case, the calculation of the chemical potential can be made 2-3 orders of magnitude more efficient than the original Siepmann scheme. Finally, Siepmann and Frenkel have shown that the Rosenbluth trial insertion scheme can be used as a starting point for a novel Monte Carlo scheme to sample equilibrium configurations of systems consisting of chain molecules [25]. A description of the latter technique would, however, fall outside the scope of the present lectures.

In view of the very rapid progress that has been made during the last 2 years in the development of novel techniques to study the chemical potential of chain molecules, it seems safe to predict that the study of phase equilibria involving long, flexible molecules will not remain a remote possibility, but become a very real one.

3.3 Overlapping distribution method

The reader may wonder why, in the previous section, we have only been discussing trial move that attempt to *add* a particle to the system, and not the reverse move. After all, the excess chemical potential can also be written as:

$$\begin{aligned} \mu &= kT \ln(Q_N/Q_{N+1}) \\ &= \mu_{id} + kT \ln \langle \exp(+\beta\Delta U) \rangle_{N+1} , \end{aligned} \quad (22)$$

where ΔU denotes the interaction energy of particle $N + 1$ with the remaining N particles. It would seem that eq. 22 can be sampled by straightforward Metropolis Monte Carlo. In general, however, this is not true. The reason is that the function $\exp(\beta\Delta U)$ is, in principle not bounded. It can become arbitrarily large, as ΔU grows. (Incidentally, this is not true for $\exp(-\beta\Delta U)$, because one of the conditions that a system must satisfy in order to be describable by classical statistical mechanics is that its the potential energy function has a lower bound). The problem with equation 22 is that very large values of the integrand coincide with very small values ($\mathcal{O}(\exp(-\beta\Delta U))$) of the Boltzmann factor (that determines

how often a configuration is sampled during a Monte Carlo run). As a consequence, an appreciable contribution to the average in eq. 22 comes from a part of configuration space that is hardly ever, or indeed never, sampled during a run. Hard spheres offer a good illustration. As the potential energy function of non-overlapping hard spheres is always zero, a simple Monte Carlo sampling of eq. 22 for a dense fluid of hard spheres would always yield the nonsensical estimate $\mu_{ex} = 0$ (whereas, in fact, at freezing, $\mu_{ex}/kT \sim 15$). The correct way to obtain chemical potentials from simulations involving both particle insertions and particle removals has been indicated by Shing and Gubbins [26, 27]. However, I find it convenient to discuss this problem in the context of a more general technique to measure free energy differences. This method was first introduced by Bennett [28] and is called the overlapping distribution method.

Consider two N -particle systems, labeled 0 and 1 with partition functions Q_0 and Q_1 . For convenience we assume that both systems have the same volume V , but this is not essential. From eqn 50 it follows that the free energy difference $\Delta F = F_1 - F_0$ can be written as:

$$\begin{aligned} \Delta F &= -kT \ln(Q_1/Q_0) \\ &= -kT \ln \left(\frac{\int ds^N \exp(-\beta U_1(\mathbf{s}^N))}{\int ds^N \exp(-\beta U_0(\mathbf{s}^N))} \right). \end{aligned} \quad (23)$$

Suppose that we are carrying out a (Metropolis) sampling of the configuration space of system 1. For every configuration visited during this sampling of system 1 we can compute the potential energy of system-0 ($U_0(\mathbf{s}^N)$) for the same configuration, and hence the potential energy difference $\Delta U = U_1(\mathbf{s}^N) - U_0(\mathbf{s}^N)$ (see figure 3). We use this information to con-



Figure 3: Example of measurement of histogram of potential energy differences (here represented by height differences) between two systems 0 and 1. Note that the two histograms will, in general, be different.

struct a histogram that measures the probability density for the potential energy difference ΔU . Let us denote this probability density by $p_1(\Delta U)$. In the canonical ensemble, $p_1(\Delta U)$ is given by:

$$p_1(\Delta U) = \frac{\int ds^N \exp(-\beta U_1) \delta(U_1 - U_0 - \Delta U)}{q_1}, \quad (24)$$

where we have denoted the scaled, configurational part of the partition function by a lower-case q (e.g. $q_1 = \int ds^N \exp(-\beta U_1(\mathbf{s}^N))$). The δ -function in eq. 24 makes that we can substitute $U_0 + \Delta U$ for U_1 in the Boltzmann factor, hence:

$$\begin{aligned} p_1(\Delta U) &= \frac{\int ds^N \exp(-\beta(U_0 + \Delta U)) \delta(U_1 - U_0 - \Delta U)}{q_1} \\ &= \frac{q_0}{q_1} \exp(-\beta \Delta U) \frac{\int ds^N \exp(-\beta U_0) \delta(U_1 - U_0 - \Delta U)}{q_0} \\ &= \frac{q_0}{q_1} \exp(-\beta \Delta U) p_0(\Delta U), \end{aligned} \quad (25)$$

where $p_0(\Delta U)$ is the probability density to find a potential energy difference ΔU between systems 1 and 0, while Boltzmann-sampling the available configurations of system 0. As the free energy difference between systems 1 and 0 is simply $\Delta F = -kT \ln(q_1/q_0)$, we find from equation 25:

$$\ln p_1(\Delta U) = \beta(\Delta F - \Delta U) + \ln p_0(\Delta U). \quad (26)$$

In order to obtain ΔF from eq. 26 in practical cases, it is convenient to define two functions f_0 and f_1 by:

$$f_0(\Delta U) = \ln p_0(\Delta U) - \frac{\beta \Delta U}{2}$$

and

$$f_1(\Delta U) = \ln p_1(\Delta U) + \frac{\beta \Delta U}{2}$$

such that

$$f_1(\Delta U) = f_0(\Delta U) + \beta \Delta F.$$

Suppose that we have measured f_0 and f_1 in two separate simulations (one sampling system 0, the other system 1). We can then obtain ΔF by fitting the functions f_0 and f_1 to two polynomials in ΔU that are identical but for the constant term. The constant offset between the two polynomials yields our estimate for ΔF . Note that, in order to perform such a fit, it is not even necessary that there exists a range of ΔU where both f_0 and f_1 can be measured. However, in the absence of such a range of overlap, the statistical accuracy of the method is usually poor.

Now consider the particle insertion/removal problem. Let us assume that system 1 is a system with N interacting particles, while system 0 contains $N - 1$ interacting particles and 1 ideal-gas particle. The difference in free energy between these two systems is obviously equal to μ_{ex} . Applying eq. 26 to this particular case, we find:

$$\Delta \mu_{ex} = f_1(\Delta U) - f_0(\Delta U). \quad (27)$$

eq. 27 is equivalent to the result obtained by Shing and Gubbins. Using the overlapping distribution method it is possible to combine the results of simulations with trial insertions and trial removals to arrive at a more accurate estimate for the chemical potential.

3.4 Umbrella sampling

In the previous section, we introduced the distribution functions $p_0(\Delta U)$ and $p_1(\Delta U)$ that measure the probability of finding system 0 (1) in an equilibrium configuration \mathbf{s}^N where its potential energy difference with system 1 (0) equals ΔU . At first sight it would seem that knowledge of either p_0 or p_1 is sufficient to estimate the free energy difference between systems 0 and 1. After all, eq. 26 states that

$$p_1(\Delta U) = p_0(\Delta U) \exp(\beta(\Delta F - \Delta U)) .$$

If we integrate over ΔU on both sides of this equation, we obtain:

$$\begin{aligned} \int_{-\infty}^{\infty} p_1(\Delta U) d\Delta U &= \exp(\beta\Delta F) \int_{-\infty}^{\infty} p_0(\Delta U) \exp(-\beta\Delta U) d\Delta U \\ 1 &= \exp(\beta\Delta F) \langle \exp(-\beta\Delta U) \rangle_0 , \end{aligned} \quad (28)$$

or

$$\exp(-\beta\Delta F) = \langle \exp(-\beta\Delta U) \rangle_0 .$$

Although eq. 28 is very useful to estimate free energy differences between two systems that are not too dissimilar, its applicability is limited. The problem is that, in many cases of practical interest, the largest contributions to the average $\langle \exp(-\beta\Delta U) \rangle_0$ come from region of configuration space where $p_0(\Delta U)$ is very small, while $\exp(-\beta\Delta U)$ is very large. As a result, the statistical error in ΔF is large.

One method to achieve a more accurate estimate of ΔF is the ‘umbrella sampling’ scheme suggested by Torrie and Valleau [29]. The basic idea behind umbrella sampling is that, in order to obtain an accurate estimate of the free energy difference between two system (0 and 1), one should sample both the part of configuration space that is accessible to system 1 and the part that is accessible to 0. In order to achieve this in a single simulation, one should modify the Markov chain that governs the sampling of configuration space. This is achieved by multiplying the Boltzmann factor of system 0 by a (positive) weighting function w . As a result, the probability of visiting a point \mathbf{q}^N in configuration space is now proportional to $\exp(-\beta U_0(\mathbf{q}^N))w(\mathbf{q}^N)$. The expression for $\langle \exp(-\beta\Delta U) \rangle_0$ now becomes:

$$\langle \exp(-\beta\Delta U) \rangle_0 = \frac{\int d\mathbf{q}^N \exp(-\beta U_0(\mathbf{q}^N))w(\mathbf{q}^N)[\exp(-\beta\Delta U(\mathbf{q}^N))/w(\mathbf{q}^N)]}{\int d\mathbf{q}^N \exp(-\beta U_0(\mathbf{q}^N))w(\mathbf{q}^N)w^{-1}(\mathbf{q}^N)} , \quad (29)$$

or, introducing the notation $\langle \dots \rangle_w$ to denote an average over a probability distribution proportional to $\exp(-\beta U_0(\mathbf{q}^N))w(\mathbf{q}^N)$:

$$\begin{aligned} \langle \exp(-\beta\Delta U) \rangle_0 &= \frac{\langle \exp(-\beta\Delta U)/w \rangle_w}{\langle 1/w \rangle_w} \\ &= \langle \exp(-\beta\Delta U)/w \rangle_w \langle w \rangle_0 . \end{aligned} \quad (30)$$

The second line of eq. 30 shows that, in order for both terms on the right-hand side of this equation to be non-zero, $p_0(\Delta U)w$ should have an appreciable overlap with $p_1(\Delta U)$, while w itself should overlap with $p_0(\Delta U)$. This ‘bridging’ property of w is responsible for the name ‘umbrella’ sampling.

Although umbrella sampling is, in principle, a powerful technique, one drawback is that the function w is not known *a priori*. Rather, it must be constructed using the available information about the functions p_0 and p_1 . This requires some skill. A second (though related) problem is that an unfortunate choice of w may result in estimates for ΔF that appear reasonable but are, in fact, wrong. Only by systematic testing is it possible to get a feeling for the statistical errors in an umbrella sampling calculation.

The following simple example is meant to demonstrate the power of the umbrella sampling technique. Consider a model for n-butane, where all bond-lengths and bond-angles are fixed, except the torsional angle ϕ . Let us assume that we know the intra-molecular energy function $U_{intra}(\phi)$ associated with changes of the conformation of the molecule. In the dilute gas, $P(\phi)$, the probability of finding a value of the torsion angle ϕ is proportional to $\exp(-\beta U_{intra}(\phi))$. For the sake of convenience, I have ignored the fact that the integration over momenta also contributes a factor to $P(\phi)$. For a discussion of this point, the reader is referred to the paper by Ryckaert in this volume. For n-butane, $P(\phi)$ has a maximum at $\phi = 0$ (the 'trans' conformation) and two lower maxima at $\phi \approx 120$ degrees, corresponding to the 'gauche' conformation. Let us suppose that we wish to know what happens to the probability to find a molecule at the 'transition state' between the two gauche conformations, when the molecule is dissolved in an atomic liquid. The total potential energy function for the molecule plus solvent is

$$U_{tot} = U_{inter}(\mathbf{q}^N, \phi_1) + U_{intra}(\phi_1).$$

The probability density $P(\phi)$ to find a particular value of the angle ϕ is now given by:

$$P(\phi) = \frac{\int \exp(-\beta U_{tot}) \delta(\phi - \phi_1) d\mathbf{q}^N d\phi_1}{\int \exp(-\beta U_{tot}) d\mathbf{q}^N d\phi_1}$$

Let us now choose the weighting function w equal to $\exp(+\beta U_{intra})$. With this choice, we can rewrite $P(\phi)$ as:

$$\begin{aligned} P(\phi) &= \frac{\int \exp(-\beta U_{tot}) w(\delta(\phi - \phi_1)/w) d\mathbf{q}^N d\phi_1}{\int \exp(-\beta U_{tot}) w w^{-1} d\mathbf{q}^N d\phi_1} \\ &= \frac{\int \exp(-\beta U_{inter}) (\delta(\phi - \phi_1) \exp(-\beta U_{intra})) d\mathbf{q}^N d\phi_1}{\int \exp(-\beta U_{inter}) \exp(-\beta U_{intra}) d\mathbf{q}^N d\phi_1} \\ &= \frac{\langle \delta(\phi - \phi_1) \exp(-\beta U_{intra}) \rangle_{inter}}{\langle \exp(-\beta U_{intra}) \rangle_{inter}}. \end{aligned} \tag{31}$$

But, as U_{intra} depends only on ϕ , we can rewrite eq. 31 as:

$$P(\phi) = \frac{\exp(-\beta U_{intra}(\phi))}{\langle \exp(-\beta U_{intra}(\phi)) \rangle_{inter}} P_{inter}(\phi),$$

where $P_{inter}(\phi)$ is the probability to find a conformation with internal angle ϕ in the absence of the intramolecular torsion barrier. $P_{inter}(\phi)$ can be computed accurately, even for values of ϕ that are very unlikely in the real system, due to the presence of the internal potential energy barrier U_{intra} .

3.5 Acceptance ratio method

Finally, we consider a scheme, derived by Bennett [28], to estimate the free energy difference between two systems (0 and 1) from two simulations: one of system 0 and one of system 1. To derive this scheme, consider the following identity:

$$\begin{aligned} \frac{Q_0}{Q_1} &= \frac{Q_0 \int w(\mathbf{q}^N) \exp(-\beta(U_0 + U_1)) d\mathbf{q}^N}{Q_1 \int w(\mathbf{q}^N) \exp(-\beta(U_0 + U_1)) d\mathbf{q}^N} \\ &= \frac{\langle w \exp(-\beta U_0) \rangle_1}{\langle w \exp(-\beta U_1) \rangle_0} \end{aligned} \quad (32)$$

eq. 32 is valid for arbitrary w . The question is: what choice of w yields the highest statistical accuracy for $\beta\Delta F = \ln(Q_0/Q_1)$? Let us first write ΔF in terms of w :

$$\beta\Delta F = \ln \langle w \exp(-\beta U_0) \rangle_1 - \ln \langle w \exp(-\beta U_1) \rangle_0 \quad (33)$$

Next we compute the estimated statistical error in $\beta\Delta F$ from the variance in the two terms on the right-hand side of eq. 33, divided by the number of (statistically independent) samples (n_0 and n_1 respectively):

$$\begin{aligned} \sigma_{\beta\Delta F}^2 &= \frac{\langle (w \exp(-\beta U_1))^2 \rangle_0 - \langle w \exp(-\beta U_1) \rangle_0^2}{n_0 \langle w \exp(-\beta U_1) \rangle_0^2} \\ &\quad + \frac{\langle (w \exp(-\beta U_0))^2 \rangle_1 - \langle w \exp(-\beta U_0) \rangle_1^2}{n_1 \langle w \exp(-\beta U_0) \rangle_1^2} \\ &= \frac{\int [(Q_0/n_0) \exp(-\beta U_1) + (Q_1/n_1) \exp(-\beta U_0)] w^2 \exp(-\beta(U_0 + U_1)) d\mathbf{q}^N}{(\int w \exp(-\beta(U_0 + U_1)) d\mathbf{q}^N)^2} \\ &\quad - \frac{1}{n_0} - \frac{1}{n_1}. \end{aligned} \quad (34)$$

Note that the right-hand side of eq. 34 does not change if we multiply w by a constant factor. We can therefore, without loss of generality, choose the following normalization for w :

$$\int w \exp(-\beta(U_0 + U_1)) d\mathbf{q}^N = \text{constant}. \quad (35)$$

Next, we minimize the statistical error in $\beta\Delta F$ with respect to w , with the constraint 35. This is done most conveniently using Lagrange multipliers:

$$\begin{aligned} 0 &= [(Q_0/n_0) \exp(-\beta U_1) + (Q_1/n_1) \exp(-\beta U_0)] \exp(-\beta(U_0 + U_1)) w \delta w \\ &\quad - \lambda \exp(-\beta(U_0 + U_1)) \delta w. \end{aligned} \quad (36)$$

or,

$$w = \frac{\text{constant}}{(Q_0/n_0) \exp(-\beta U_1) + (Q_1/n_1) \exp(-\beta U_0)} \quad (37)$$

If we now insert this expression for w in eq. 32, we obtain:

$$\frac{Q_0}{Q_1} = \frac{\langle [1 + \exp(\beta(U_0 - U_1 + C))]^{-1} \rangle}{\langle [1 + \exp(\beta(U_1 - U_0 - C))]^{-1} \rangle} \exp(-\beta C) \quad (38)$$

where we have defined $\exp(\beta C) \equiv (Q_0 n_1)/(Q_1 n_0)$. We can express eq. 38 in terms of the Fermi-Dirac function $f(x) \equiv 1/(1 + \exp(\beta x))$:

$$\frac{Q_0}{Q_1} = \frac{\langle f(U_0 - U_1 + C) \rangle_1}{\langle f(U_1 - U_0 - C) \rangle_0} \exp(-\beta C) \quad (39)$$

Note that eq. 39 is valid for any choice of C . However, the choice $C = \ln[(Q_0 n_1)/(Q_1 n_0)]$ is optimal.

At first sight this choice of C seems problematic because it presupposes knowledge of the very quantity we wish to compute, *viz.* (Q_0/Q_1) . In practice, C is determined by a self-consistency requirement, described below.

Suppose that we have obtained numerical estimates for $\langle f(U_0 - U_1 + C) \rangle_1$ and $\langle f(U_1 - U_0 - C) \rangle_0$ for a range of values of C :

$$\begin{aligned} \langle f(U_0 - U_1 + C) \rangle_1 &= \frac{1}{n_1} \sum_m f_m(U_0 - U_1 + C) \\ \langle f(U_1 - U_0 - C) \rangle_0 &= \frac{1}{n_0} \sum_{m'} f_{m'}(U_1 - U_0 - C) \end{aligned} \quad (40)$$

where \sum_m ($\sum_{m'}$) stands for the sum over all configurations sampled in a Monte Carlo simulation of system 1 (0). Inserting eqs. 40 and 39 in eq. 33, we obtain:

$$\beta \Delta F = \ln \frac{\sum_1 f(U_0 - U_1 + C)}{\sum_0 f(U_1 - U_0 - C)} - \ln(n_1/n_0) + \beta C \quad (41)$$

while the optimal choice for C can be rewritten as:

$$\beta \Delta F = -\ln(n_1/n_0) + \beta C \quad (42)$$

Clearly, eq. 41 and eq. 42 are consistent only if

$$\sum_m f(U_0 - U_1 + C) = \sum_{m'} f(U_1 - U_0 - C) \quad (43)$$

In practical situations, C will be treated as an adjustable parameter that is varied until eq. 43 is satisfied. For that value of C , $\beta \Delta F$ then follows immediately from eq. 42.

3.6 Particle removal and vacancies

I end this discussion of particle insertion techniques by considering the opposite, namely the formation of a vacancy in a solid. In order to see what we must compute in order to be able to estimate the equilibrium concentration of vacancies in a solid, consider the Grand-Canonical (GC) ensemble. The GC partition function is

$$\Xi = \sum_N \frac{q^N(T) \exp(\beta \mu N)}{N!} \int d\mathbf{q}^N \exp(-\beta U(\mathbf{q}^N)), \quad (44)$$

where $U(\mathbf{q}^N)$ denotes the potential energy function of a system of N particles and $q(T)$ is the 'kinetic' contribution to the partition function. Let us consider that the system under

study is in a crystalline phase. For a given value of μ , the equilibrium density of the crystal is well defined. Let us assume that the number of Wigner-Seitz cells in a volume V is given by N_0 . Clearly, N , the actual number of atoms in the crystal may be either less than N_0 (vacancies) or larger (interstitials). Let us focus on the vacancies. In that case, we can write $N = N_0 - n$, where n is the number of vacancies. How many vacancies are there? To see this we must find the largest term in eq. 44, i.e. the one that corresponds to the most likely value of N . To find this term, we rewrite eq. 44 by factoring out the term corresponding to a lattice free of vacancies:

$$\Xi = Q(N_0, V, T) \exp(\beta\mu N_0) \sum_{n=0}^{N_0} \times \quad (45)$$

$$\left(\frac{N_0!}{(N_0 - n)!n!} \right) q^{-n}(T) \exp(-\beta\mu n) \frac{\int d\mathbf{q}^{N_0-n} \exp(-\beta U(\mathbf{q}^{N_0-n}))}{\int d\mathbf{q}^{N_0} \exp(-\beta U(\mathbf{q}^{N_0}))}.$$

We now assume that the number of vacancies, n , is much smaller than N_0 . This is a reasonable assumption, because if it were not true, we would not have a mechanically stable crystal. As the concentration of vacancies is low, we can write:

$$\frac{\int d\mathbf{q}^{N_0-n} \exp(-\beta U(\mathbf{q}^{N_0-n}))}{\int d\mathbf{q}^{N_0} \exp(-\beta U(\mathbf{q}^{N_0}))} \approx \left(\frac{\int d\mathbf{q}^{N_0-1} \exp(-\beta U(\mathbf{q}^{N_0-1}))}{\int d\mathbf{q}^{N_0} \exp(-\beta U(\mathbf{q}^{N_0}))} \right)^n \quad (46)$$

To find the maximum term, we equate the logarithmic derivative of the n -th term in the sum to 0:

$$0 = \ln \left(\frac{N_0}{n} \right) - \ln q(T) - \beta\mu + \ln \left(\frac{\int d\mathbf{q}^{N_0-1} \exp(-\beta U(\mathbf{q}^{N_0-1}))}{\int d\mathbf{q}^{N_0} \exp(-\beta U(\mathbf{q}^{N_0}))} \right)$$

or

$$\frac{n}{N_0} = \frac{\exp(-\beta\mu)}{q(T)} \left(\frac{\int d\mathbf{q}^{N_0-1} \exp(-\beta U(\mathbf{q}^{N_0-1}))}{\int d\mathbf{q}^{N_0} \exp(-\beta U(\mathbf{q}^{N_0}))} \right) \quad (47)$$

This expression shows that the vacancy concentration depends on two factors: first of all on the chemical potential of the particles in the crystal (or actually, on the fugacity) and secondly on the ratio of the configurational integral of a system with 0 and 1 vacancy. This latter ratio should be computed by particle ‘removal’, but we know from the previous sections that there are better ways to compute it. For more details, the reader is referred to refs. [30, 31, 32].

4 Other ensembles

Thus far I have focused on techniques to locate first order phase transitions by direct calculation of the chemical potential in the two coexisting phases. However, under certain conditions, it is possible to study phase coexistence much more directly by performing simulations in another ensemble than the canonical (N, V, T fixed). In order to explain Monte Carlo simulations in these other ensembles, I first discuss the simplest example, i.e. the isothermal-isobaric (N, P, T fixed) ensemble. The introduction of this ensemble will help me to define the terminology that I will use later on to discuss the more sophisticated ensembles that are used to study first-order phase transitions.

4.1 Isobaric-isothermal ensemble

Constant-pressure Monte Carlo simulations were first described by Wood [33] in the context of a simulation-study of two-dimensional hard disks. Although the method introduced by Wood is very elegant, it is not readily applied to systems with arbitrary continuous potentials. McDonald [34] was the first to apply constant- NPT simulations to a system with continuous intermolecular forces (a Lennard-Jones mixture), and it is the constant-pressure method of McDonald that is now being used almost universally, and that is discussed below.

I will derive the basic equations of constant-pressure Monte Carlo in a way that may appear unnecessarily complicated. However, this derivation has the advantage that the same framework can be used to introduce some of the other non- NVT Monte Carlo methods to be discussed below. For the sake of convenience I shall initially assume that we are dealing with a system of N identical atoms. The partition function for this system is given by:

$$Q(N, V, T) = \frac{q^N(T)}{N!} \int_0^L \cdots \int_0^L d\mathbf{q}^N \exp(-\beta U(\mathbf{q}^N)). \quad (48)$$

It is convenient to rewrite eq. 48 in terms of the scaled coordinates \mathbf{s} :

$$Q(N, V, T) = \frac{(q(T)V)^N}{N!} \int_0^1 \cdots \int_0^1 ds^N \exp(-\beta U(\mathbf{s}^N; L)). \quad (49)$$

In equation 49, we have written $U(\mathbf{s}^N; L)$ to indicate that U depends on the *real* rather than the *scaled* distances between the particles. The expression for the Helmholtz free energy of the system is:

$$\begin{aligned} F(N, V, T) &= -kT \ln Q \\ &= -kT \ln \left(\frac{(q(T)V)^N}{N!} \right) - kT \ln \left(\int ds^N \exp[-\beta U(\mathbf{s}^N; L)] \right) \\ &= F_{id}(N, V, T) + F_{ex}(N, V, T). \end{aligned} \quad (50)$$

In the last line of the above equation we have identified the two contributions to the Helmholtz free energy on the previous line as the ideal-gas expression plus an excess part. Let us now assume that the system is separated by a 'piston' [35] from an ideal gas reservoir (see figure 4). The total volume of the system plus reservoir is fixed at a value V_0 . The total number of particles is M . Hence the volume accessible to the $m \equiv M - N$ ideal gas molecules is $V_0 - V$. The partition function of the total system is simply the product of the partition functions of the constituent sub-systems:

$$Q(N, m, V, V_0, T) = \frac{q^M V^N (V_0 - V)^m}{N! m!} \int ds^m \int ds^N \exp(-\beta U(\mathbf{s}^N; L)). \quad (51)$$

Note that the integral over the \mathbf{s}^m scaled coordinates of the ideal gas yields simply 1. For the sake of compactness we have assumed that the thermal wavelength of the ideal gas molecules is also equal to Λ . The total free energy of this combined system is $F_{tot} = -kT \ln Q(N, m, V, V_0, T)$. Now let us assume that the 'piston' between the two subsystems is free to move, so that the volume V of the N -particle subsystem can fluctuate. Of course, the most probable value of V will be the one that minimizes the free energy of the combined

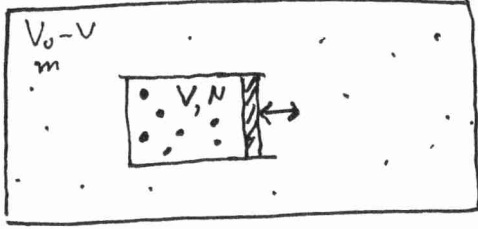


Figure 4: Ideal gas (m particles, volume $V_0 - V$) can exchange volume with an N -particle system (volume V)

system. The probability density $\mathcal{P}(V)$ that the N -particle subsystem has a volume V is given by:

$$\mathcal{P}(V) = \frac{V^N (V_0 - V)^m \int d\mathbf{s}^N \exp(-\beta U(\mathbf{s}^N; L))}{\int_0^{V_0} dV' V'^N (V_0 - V')^m \int d\mathbf{s}^N \exp(-\beta U(\mathbf{s}^N; L'))} \quad (52)$$

We now consider the limit that the size of the reservoir tends to infinity ($V_0 \rightarrow \infty, M \rightarrow \infty, (m/V_0 \rightarrow \rho)$). In that limit, a small volume change of the small system does not change the pressure P of the large system. In other words, the large system works as a manostat for the small system. In that case we can simplify eqs. 51 and 52. Note that in the limit $V/V_0 \rightarrow 0$ we can write:

$$(V_0 - V)^m = V_0^m (1 - (V/V_0))^m \rightarrow V_0^m \exp(-mV/V_0).$$

Note that for $m \rightarrow \infty$, $\exp(-mV/V_0) \rightarrow \exp(-\rho V)$. But, as the reservoir contains an ideal gas, ρ can be written as βP . With these substitutions, eq. 52 becomes:

$$\mathcal{P}(V) = \frac{V^N \exp(-\beta PV) \int d\mathbf{s}^N \exp(-\beta U(\mathbf{s}^N; L))}{\int_0^{V_0} dV' V'^N \exp(-\beta PV') \int d\mathbf{s}^N \exp(-\beta U(\mathbf{s}^N; L'))}. \quad (53)$$

In the same limit, the difference in free energy between the combined system and the ideal-gas system in the absence of the N -particle subsystem is the well-known Gibbs free energy G :

$$G(N, P, T) = -kT \ln \int dV \frac{V^N \exp(-\beta PV)}{\Lambda^{3N} N!} \int d\mathbf{s}^N \exp(-\beta U(\mathbf{s}^N; L)) \quad (54)$$

Equation 53 is the starting point for constant- NPT Monte Carlo simulations. The idea is that the probability-density to find the small system in a particular configuration of the N atoms (as specified by \mathbf{s}^N) at a given volume V is given by:

$$\mathcal{P}(V; \mathbf{s}^N) = \frac{V^N \exp(-\beta PV) \exp(-\beta U(\mathbf{s}^N; L))}{\int_0^{V_0} dV' V'^N \exp(-\beta PV') \int d\mathbf{s}^N \exp(-\beta U(\mathbf{s}^N; L'))}.$$

We can now carry out Metropolis sampling on the reduced coordinates \mathbf{s} and the volume V , with a weight-function $\rho(\mathbf{s}^N, V)$ proportional to $\exp(-\beta\{U(\mathbf{s}^N, V) + PV - N\beta^{-1} \ln V\})$. In the constant- N, P, T MC method, V is simply treated as an additional coordinate, and trial moves in V must satisfy the same rules as trial moves in \mathbf{q} (in particular, we should

maintain the symmetry of the underlying Markov chain). Let us assume that our trial moves consist of an attempted change of the volume from V to $V' = V + \Delta V$, where ΔV is a random number uniformly distributed between over the interval $[-\Delta V_{max}, +\Delta V_{max}]$. In the Metropolis scheme such a random, volume changing move will be accepted if:

$$\exp(-\beta[U(\mathbf{s}^N, V') - U(\mathbf{s}^N, V) + P(V' - V) - N\beta^{-1} \ln(V'/V)]) > \mathcal{R}, \quad (55)$$

where \mathcal{R} is a random number, uniformly distributed over the interval $[0, 1]$. Instead of attempting random changes in the volume itself, one might construct trial moves in the box-length L [34], or in the logarithm of the volume [36]. Such trial moves are equally legitimate, as long as the symmetry of the underlying Markov chain is maintained. However, such alternative schemes result in a slightly different form for eq. 55.

4.2 Grand canonical ensemble

The Metropolis sampling scheme is a method to compute thermal averages of functions $A(\mathbf{q}^N)$, that depend explicitly on the coordinates of the molecules in the N -body system under study. Examples of such ‘mechanical’ properties are the potential energy or the virial contribution to the pressure. However, the Metropolis method cannot be used to determine the integral $\int d\mathbf{q}^N \exp(-\beta U(\mathbf{q}^N))$ itself. The latter quantity measures the effective volume in configuration space that is accessible to the system. Hence the original Metropolis scheme could not be used to determine those thermodynamic properties of a system that depend explicitly on the configurational integral. However, although the Metropolis method cannot be used to measure, for instance, free energies directly, it can be used to measure the *difference* in free energy between two possible states of an N -body system. This fact is exploited in the Grand-Canonical Monte Carlo method (GCMC) developed first implemented for classical fluids by Norman and Filinov [37], and later extended and improved by a number of other groups [38, 39, 40, 41, 42, 43, 44, 45, 46]. The basic idea of the GCMC method is explained below.

In order to understand the statistical mechanical basis for the GCMC technique, let us return to eq. 51 of section 4.1. This equation gives the partition function of a combined system of N interacting particles in volume V and $m = M - N$ ideal gas molecules in volume $V_0 - V$:

$$Q(N, m, V, V_0, T) = \frac{V^N (V_0 - V)^m}{\Lambda^{3M} N! m!} \int d\mathbf{s}^m \int d\mathbf{s}^N \exp(-\beta U(\mathbf{s}^N)). \quad (51)$$

Now, instead of allowing the two systems to exchange volume, let us see what happens if the systems can exchange particles (see figure 5). To be more precise, we assume that the molecules in the two sub-volumes are actually identical particles. The only difference is that when they find themselves in volume V they interact and when they are in volume $V_0 - V$, they do not. If we transfer a molecule i from a reduced coordinate \mathbf{s}_i in the volume $V_0 - V$ to the same reduced coordinate in volume V , then the potential energy function U changes from $U(\mathbf{s}^N)$ to $U(\mathbf{s}^{N+1})$. The expression for the total partition function of the system, including all possible distributions of the M particles over the two sub-volumes is:

$$Q(M, V, V_0, T) = \sum_{N=0}^M \frac{V^N (V_0 - V)^{M-N}}{\Lambda^{3M} N! (M - N)!} \int d\mathbf{s}^{M-N} \int d\mathbf{s}^N \exp(-\beta U(\mathbf{s}^N)). \quad (56)$$

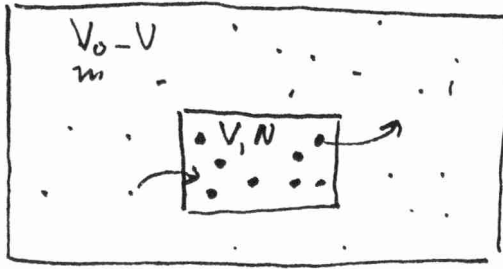


Figure 5: Ideal gas (m particles, volume $V_0 - V$) can exchange particles with an N -particle system (volume V)

Following the approach of section 4.1, we now write the probability density to find a system with $M - N$ particles at reduced coordinates \mathbf{s}^{M-N} in volume $V' \equiv V_0 - V$ and N particles at reduced coordinates \mathbf{s}^N in volume V :

$$\mathcal{P}(\mathbf{s}^M; N) = \frac{V^N V'^{M-N}}{Q(M, V, V', T) \Lambda^{3M} N! (M - N)!} \exp(-\beta U(\mathbf{s}^N)). \quad (57)$$

Let us now consider a trial move in which a particle is transferred from V' to the same scaled coordinate in V . First we should make sure that we construct an underlying Markov chain that is symmetric. Symmetry, in this case, implies that the *a priori* probability to move a particle from V' to V should be equal to the *a priori* probability of the reverse move. The probability of acceptance of a trial move in which we move a particle *to* or *from* volume V is determined by the ratio of the corresponding probability densities (eq. 57):

$$P_{N \rightarrow N+1} = \frac{V(M - N)}{V'(N + 1)} \exp(-\beta(U(\mathbf{s}^{N+1}) - U(\mathbf{s}^N))) \quad (58)$$

$$P_{N+1 \rightarrow N} = \frac{V'(N + 1)}{V(M - N)} \exp(-\beta(U(\mathbf{s}^N) - U(\mathbf{s}^{N+1}))). \quad (59)$$

Now let us consider the limit that the ideal gas system is very much larger than the interacting system: $M \rightarrow \infty, V' \rightarrow \infty, (M/V') \rightarrow \rho$. Note that for an ideal gas the chemical potential μ is related to the particle-density ρ by: $\mu = kT \ln \Lambda^3 \rho$. Therefore, in the limit $(M/N) \rightarrow \infty$, eqs. 58- 59 become:

$$P_{N \rightarrow N+1} = \frac{V}{N + 1} \Lambda^{-3} \exp(\beta\mu) \exp(-\beta(U(\mathbf{s}^{N+1}) - U(\mathbf{s}^N))) \quad (60)$$

$$P_{N+1 \rightarrow N} = \frac{(N + 1)}{V} \Lambda^3 \exp(-\beta\mu) \exp(-\beta(U(\mathbf{s}^N) - U(\mathbf{s}^{N+1}))). \quad (61)$$

In the Metropolis scheme, an attempted particle addition to (removal from) volume V is accepted if $P_{N \rightarrow N+1} > \mathcal{R}$ ($P_{N+1 \rightarrow N} > \mathcal{R}$), where \mathcal{R} is a random number uniformly distributed in the interval $[0, 1]$.

Equations 60- 61 are the basic equations for Grand Canonical Monte Carlo simulations. Acceptable trial moves are: *i*) the random insertion of an additional particle at any point in volume V , *ii*) the random removal of any of the N particles in volume V . In addition, the

particles in volume V can sample the accessible configuration-space by conventional Monte Carlo sampling. Note that in equations 60- 61 all explicit reference to the ideal-gas system has disappeared. The rules only refer to the system of volume V .

The most salient feature of the GCMC technique is that in such simulations the chemical potential μ is *imposed*, while the number of particles N is a fluctuating quantity. During the simulation we may measure other thermodynamic quantities, such as the pressure P , the average density $\langle \rho \rangle$ or the internal energy $\langle U \rangle$. As we know μ , we can derive all other ‘thermal’ properties, such as the Helmholtz free energy or the entropy. This may seem surprising. After all, in section 1 we stated that Monte Carlo sampling *cannot* be used to sample absolute free energies and related quantities. Yet, with Grand Canonical MC we appear to be doing precisely that. The answer is that, in fact, we do not. What we measure is not an absolute but a relative free energy. In GCMC, we are equating the chemical potential of a molecule in an ideal gas at density ρ (for the ideal-gas case we know how to compute μ) and the chemical potential of the same species in an interacting system at density ρ' .

Grand canonical MC works best if the acceptance of trial moves by which particles are added or removed is not too low. For atomic fluids this condition effectively limits the maximum density at which the method can be used to about twice the critical density. Special tricks are needed to extend GCMC to somewhat higher densities [44]. GCMC is easily implemented for mixtures and inhomogeneous systems, such as fluids near interfaces. In fact, some of the most useful applications of the GCMC method are precisely in these areas of research. Although GCMC can be applied to simple models of non-spherical molecules, the conventional approach converges poorly for all but the smallest polyatomic molecules (see however, section 3.2). For more details on the Grand Canonical Monte Carlo method, the reader is referred to the book by Allen and Tildesley [47] and a review paper by Frenkel [16]. Quite recently, a scheme has been proposed to perform *Molecular Dynamics* calculations in the grand-canonical ensemble [48]. The advantage of this approach is that particles can be added or removed continuously.

4.3 Gibbs ensemble

As was already mentioned in the introduction, the condition for coexistence of two or more phases I, II, \dots is that the pressure of all coexisting phases must be equal ($P_I = P_{II} = \dots = P$), as must be the temperature ($T_I = T_{II} = \dots = T$) and the chemical potentials of all species ($\mu_I^\alpha = \mu_{II}^\alpha = \dots = \mu^\alpha$). Hence one might be inclined to think that the best ensemble to study would be the ‘constant- μPT ensemble’. The quotation marks around the name of this ‘ensemble’ are intentional, because, strictly speaking, no such ensemble exists. The reason is simple: if we specify only intensive parameters, such as P, T and μ , the extensive variables (such as V) are unbounded. Another way to say the same thing is that the set P, T, μ is linearly dependent. In order to get a decent ensemble, we must fix at least one extensive variable. In the case of constant-pressure MC this variable is the number of particles N , while in Grand Canonical Monte Carlo the volume V of the system is fixed.

Recently, however, Panagiotopoulos [49] has developed a new Monte Carlo scheme, called the ‘Gibbs method’, that comes very close to achieving the impossible: namely

simulating phase equilibria under conditions where the pressure, temperature and chemical potential(s) of the coexisting phases are equal. The reason that this method can work is that, although the *difference* between chemical potentials in different phases is fixed (namely, at $\Delta\mu = 0$), the absolute values are still free to change. Below we shall show how the Gibbs method can be derived using the description developed in the previous sections.

We start our discussion by recalling the expression for the partition function for a system of M particles distributed over two volumes V and $V' = V_0 - V$, i.e. eq. 56 in section 4.2:

$$Q(M, V, V', T) = \sum_{N=0}^M \frac{V^N V'^{M-N}}{\Lambda^{3M} N!(M-N)!} \int ds^{M-N} \int ds^N \exp(-\beta U(\mathbf{s}^N)).$$

In the previous section we assumed that the particles in volume V' behaved as ideal-gas molecules. Now we consider the case that the particles in both volumes are subject to the same intermolecular interactions. In that case, the partition function becomes:

$$Q(M, V, V', T) = \sum_{N=0}^M \frac{V^N V'^{M-N}}{\Lambda^{3M} N!(M-N)!} \int ds^{M-N} \exp(-\beta U(\mathbf{s}^{M-N})) \int ds^N \exp(-\beta U(\mathbf{s}^N)). \quad (62)$$

We now allow trial moves to transport particles from one sub-system to the other (see figure 6). Using the results of the previous section, it is easy to see that the probability

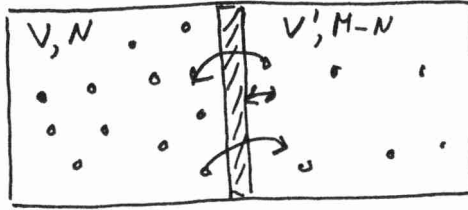


Figure 6: Gibbs ensemble. Two systems can exchange both volume and particles. But the total volume and the total number of particles is fixed.

ratio associated with a trial move that transfers one particle from volume V' to volume V is given by:

$$P_{N \rightarrow N+1} = \frac{V(M-N)}{V'(N+1)} \exp(-\beta[U(\mathbf{s}^{N+1}; V) - U(\mathbf{s}^N; V) + U(\mathbf{s}^{M-N-1}; V') - U(\mathbf{s}^{M-N}; V')]). \quad (63)$$

The corresponding expression for the reverse trial move follows by making the appropriate substitutions in eq. 64. As before, the acceptance or rejection of this trial move can be decided by comparing $P_{N \rightarrow N+1}$ with a random number in the interval $[0, 1]$. At this stage, we could set up a Monte Carlo simulation in which we allow trial moves that transfer particles from V to V' and *vice versa*. In the course of such a simulation, the distribution

of particles over V and V' would become such that both subsystems are at the same chemical potential. This may correspond to a situation where both subsystems have the same density and pressure, but this need not be the case. For example, if the overall density of the total system (M/V_0), corresponds to a point in the two-phase region of a first-order phase transition, the two sub-systems may end up in different phases (which is desirable), at different pressures (which is undesirable). In order to ensure that the two subsystems are always at the same pressure, the Gibbs method also allows for volume changing moves. These may either keep the total volume V_0 fixed (this was the formulation of the original paper of Panagiotopoulos [49]), or the two systems may both be in contact with a constant-pressure bath at pressure P (this generalization is described in a subsequent paper by Panagiotopoulos et al. [50]). Both methods follow directly from the discussion in section 4.1. For the sake of completeness we write down the expressions for the probability ratios associated with a volume-changing move in the constant- V_0 ensemble:

$$\begin{aligned}
 P(V \rightarrow V + \Delta V, V' \rightarrow V' - \Delta V) = \\
 \exp(-\beta[U_N(V + \Delta V) - U_N(V) + U_{M-N}(V' - \Delta V) - U_{M-N}(V')]) \cdot \\
 \exp[N \ln((V + \Delta V)/V) + (M - N) \ln((V' - \Delta V)/V')] .
 \end{aligned} \tag{64}$$

In the constant- P ensemble volume changing moves on the two subsystems can be carried out independently. The probability of acceptance of such trial moves is given directly by eq. 55 of section 4.1. Of course, this constant- P method can only be applied to systems containing two or more components because in a one-component system, the two-phase region is a *line* in the $P - T$ -plane. Hence, the probability that any specific choice of P and T will actually be *at* the phase transition, is vanishingly small. In contrast, for two-component systems, the two-phase region corresponds to a finite *area* in the $P - T$ -plane.

Note that in either formulation of the Gibbs method, the total number of particles is fixed. The method can be extended to study inhomogeneous systems [51] and is particularly suited to study phase equilibria in multicomponent mixtures and equilibria across semi-permeable membranes [50]. The great advantage of the Gibbs method over the conventional techniques to study phase-coexistence is that in the Gibbs method the system spontaneously ‘finds’ the densities and compositions of the coexisting phases. In contrast, the conventional approach was, for instance, to compute the relevant chemical potentials as a function of pressure at a number of different compositions (this might require an appreciable number of simulations), and then *construct* the coexistence line.

At the beginning of this section I stated that the Gibbs ensemble is *not* a ‘constant- μ, P, T ’ ensemble, but I did not say what ensemble it actually corresponds to. This point has been considered by Smit et al. [52] who concluded that, in the thermodynamic limit, the (constant- V) ‘Gibbs’ ensemble is rigorously equivalent to the canonical ensemble. At present, the Gibbs ensemble method has become the technique *par excellence* to study fluid-fluid phase equilibria. However, like the Grand-canonical ensemble scheme, the method does rely on a reasonable number of successful particle insertions to achieve compositional equilibrium. As a consequence, the Gibbs ensemble method cannot be used to study phase equilibria involving very dense phase or crystalline solids. Although there exist, to my knowledge, no numerical schemes that allow *direct* simulation of, say, solid-liquid phase coexistence in a multicomponent system, there exists a technique that greatly facilitates

the numerical study of such phase equilibria. This is the so-called ‘Semi-Grand ensemble method’ of Kofke and Glandt [53]. In this next section, I shall present a simple description of this method.

4.4 Semi-grand ensemble

In order to understand why the semi-grand ensemble can be successful where other schemes fail, it is instructive to return to the particle insertion method described in section 3.1. In that section, we saw that the excess chemical potential of a molecule in a fluid is related to the average Boltzmann factor associated with the random addition of such a molecule to a fluid with N particles present (eq. 9):

$$\mu_{ex} = -kT \ln \left\langle \int ds_{N+1} \exp(-\beta\Delta U) \right\rangle_N .$$

Let us assume that we wish to study phase equilibria in a binary mixture. In that case, we must compute the Gibbs free energy per mole of the mixture, as a function of the composition:

$$G(X_A) = X_A \mu_A + X_B \mu_B , \quad (65)$$

where $X_A (=1-X_B)$ denotes the mole-fraction of species A , and μ_A (μ_B) denote the chemical potentials of the two components in the mixture. Let us assume that we have somehow succeeded in computing the Gibbs free energy of one of the pure phases (for instance, by one of the thermodynamic integration methods described in section 2). At first sight it might seem that, in order to compute G as a function of X_A , we have to repeat such a thermodynamic integration for a large number of X_A values. Fortunately, this is usually not the case. Rather than recomputing $G(X)$ for a number of compositions, we can study the *change* in $G(X)$ with X . In other words, we need to have a ‘microscopic’ expression for

$$\begin{aligned} \left(\frac{\partial G(X)}{\partial X} \right)_{P,T,N} &= \mu_A - \mu_B \\ &= (\mu_A - \mu_B)_{id} + (\mu_A - \mu_B)_{ex} . \end{aligned} \quad (66)$$

In the first line of eq. 66, we have used the Gibbs-Duhem relation. I assume that the ideal-gas contributions to the chemical potential of both A and B are known. The quantity that we must compute is $\Delta\mu_{ex} \equiv (\mu_A - \mu_B)_{ex}$. Naively, one might try to measure this quantity by using the particle insertion method to obtain μ_{ex} of species A and B separately and then subtracting the result. Although such an approach would be correct *in principle*, it is time consuming and not very accurate. Fortunately, $\Delta\mu_{ex}$ can be obtained much more directly by measuring the Boltzmann factor associated with a virtual trial move where a randomly selected particle of type B is transformed into a particle of type A [13, 15]. I leave it as an exercise to the reader to derive that the resulting expression for $\Delta\mu_{ex}$ at constant pressure is:

$$\Delta\mu_{ex} = -k_B T \ln \left\langle \frac{N_B}{N_A + 1} \exp(-\beta\Delta U^{+-}) \right\rangle \quad (67)$$

where ΔU^{+-} denotes the change in potential energy of the system if one particle of type B is changed into type A . $-k_B T \ln(N_B/[N_A + 1])$ is simply the ideal mixing contribution

to the chemical potential. The point to note about eq. 67 is that for a perfect mixture (i.e. A and B have the same intermolecular interactions), $\ln < \exp -\beta \Delta U^{+-} >$ is identically equal to zero. In other words, we may obtain very good statistics on $\Delta \mu_{ex}$ even when the direct measurement of the excess chemical potential of the individual species would yield poor statistics.

The aim of this introduction to the semi-grand ensemble is twofold: first of all, eq. 67 shows that the Boltzmann factor associated with the change of identity of a particle in a mixture is related to the difference in excess chemical potential of the two species that take part in the interchange. And secondly, I have made it plausible that we can get good statistics on $\Delta \mu_{ex}$ even when the particle insertion method to measure the excess chemical potential of the individual species fails, for instance in a crystalline solid [11]. I recall that the grand-canonical Monte Carlo method has about the same range of applicability as the particle insertion method. It is therefore logical to infer that it should be possible to construct a simulation scheme based on particle *interchanges* that should work under conditions where the GCMC scheme fails. The semi-grand canonical Monte Carlo (SGCMC) method is such a scheme.

How does the SGCMC method work? Let us first consider the expression for Ξ , the grand-canonical partition function for an n -component mixture:

$$\Xi = \sum_{N_1, N_2, \dots, N_n}^{\infty} \prod_{i=1}^n \frac{q_i^{N_i} \exp(\beta \mu_i N_i)}{N_i!} V^N \int d\mathbf{s}^N \exp(-\beta U(\mathbf{s}^N)), \quad (68)$$

where $N \equiv \sum_i N_i$, $U(\mathbf{s}^N)$ denotes the potential energy function of the n -component mixture and q_i is the ‘kinetic’ contribution to the partition function due to species i . Next, we consider a related partition function Ξ' , identical to Ξ , but for the fact that we have imposed the constraint that $N = \sum_i N_i$ is fixed. If N is fixed, we can eliminate one of the N_i , for instance N_1 , from the sum in equation 68 and we obtain:

$$\Xi' = \sum_{N_2, \dots, N_n}^{\prime} q_1^N \exp(\beta \mu_1 N) \prod_{i=1}^n \left(\frac{q_i}{q_1} \right)^{N_i} \frac{\exp(\beta(\mu_i - \mu_1)N_i)}{N_i!} V^N \int d\mathbf{s}^N \exp(-\beta U(\mathbf{s}^N)). \quad (69)$$

We now multiply this equation on both sides by $\exp(-\beta \mu_1 N)$ and we define a new partition function $\mathcal{Y} \equiv \Xi' \exp(-\beta \mu_1 N)$:

$$\mathcal{Y} = \sum_{N_2, \dots, N_n}^{\prime} q_1^N \prod_{i=1}^n \left(\frac{q_i}{q_1} \right)^{N_i} \frac{\exp(\beta(\mu_i - \mu_1)N_i)}{N_i!} V^N \int d\mathbf{s}^N \exp(-\beta U(\mathbf{s}^N)). \quad (70)$$

The next step is subtle. We shall reinterpret the sum over all N_i in eqs. 68-70. In these equations, we had assumed that to every composition N_1, N_2, \dots, N_n , there corresponds *one* term in the sum. Let us now take a somewhat different point of view: we assume that all these different species are all manifestations of one and the same ‘particle’. This sounds strange, so I shall use an analogy to explain what I mean. Let us consider that we have group of 100 people, made up a 3 groups: eaters, drinkers and sleepers. In fact, we want to consider all possible combinations of these groups, with the constraint that the total number is fixed. One such combination would be: 30 eaters, 30 drinkers and 40 sleepers.

Now we make a discovery: one and the same person can be an eater, a drinker or a sleeper, but not simultaneously. Now our sum over all combinations becomes different: we have 100 ‘persons’ who can all take on any one out of the three possible identities. In that case, we have many more ways in which we can make a group of 30 eaters, 30 drinkers and 40 sleepers, namely $100!/(30!30!40!)$. If we wish to have the same total number of terms in our sum as before, we have to divide by this factor.

Let us now translate this example back to the sum over particles in eq. 70. We replace the sum over numbers of particles of species i , by a sum over all possible identities of all particles. But then we must correct for double counting by dividing by $N!/(N_1! \times \dots \times N_n!)$. If we do that, eq. 70 becomes:

$$\mathcal{Y} = \sum_{\text{identities}} \frac{q_1^N}{N!} \prod_{i=1}^n \left(\frac{q_i}{q_1} \right)^{N_i} \exp(\beta(\mu_i - \mu_1)N_i) V^N \int ds^N \exp(-\beta U(\mathbf{s}^N)). \quad (71)$$

Finally, it turns out that it is more convenient to consider the corresponding ensemble at constant pressure. In that case, the partition function changes to

$$\mathcal{Y}' = \beta P \int dV \exp(-\beta PV) \frac{(Vq_1)^N}{N!} \times \left(\sum_{\text{identities}} \prod_{i=1}^n \left(\frac{q_i}{q_1} \right)^{N_i} \exp(\beta(\mu_i - \mu_1)N_i) \int ds^N \exp(-\beta U(\mathbf{s}^N)) \right). \quad (72)$$

For cosmetic reasons, we rewrite eq. 72 in terms of the *fugacities* f_i , rather than the chemical potentials μ_i . Recall that the fugacity of a species i is defined by the expression:

$$\mu_i(P, T, \{X_i\}) \equiv \mu_i^0(T) + k_B T \ln(f_i), \quad (73)$$

where $\mu_i^0(T)$ is the chemical potential of the ideal gas reference state ($P = 1$) of species i . Using the expression for the chemical potential of an ideal gas at pressure P , and recalling that for an ideal gas $f = P$, it is easy to show that:

$$\mu_i^0(T) = -k_B T \ln(k_B T q_i). \quad (74)$$

Inserting eq. 74 in eq. 72, we obtain:

$$\mathcal{Y}' = \beta P \int dV \exp(-\beta PV) \frac{(Vq_1)^N}{N!} \sum_{\text{identities}} \prod_{i=1}^n \left(\frac{f_i}{f_1} \right)^{N_i} \int ds^N \exp(-\beta U(\mathbf{s}^N)). \quad (75)$$

By now the reader is probably thoroughly confused by all the algebra. In order to see what we have done, it is instructive to look at the characteristic thermodynamic function associated with the successive partition functions. We started with a Grand-Canonical ensemble. The link with thermodynamics is given by:

$$\beta PV = \ln \Xi(V, T, \{\mu_i\}). \quad (76)$$

The transformation to \mathcal{Y} (equation 70), corresponds to a change to the thermodynamic variable

$$\beta(PV - \mu_1 N) = \ln \mathcal{Y}(V, T, N, \{\mu_i | i \neq 1\}). \quad (77)$$

Finally, we change to constant pressure, which means that the characteristic thermodynamic function becomes:

$$\beta\mu_1 N = -\ln \mathcal{Y}'(P, T, \{\ln(f_i/f_1) | i \neq 1\}). \quad (78)$$

Rather than use $\ln(f_i/f_1)$ as the independent variable, it is more convenient to follow ref. [53] and use the *fugacity fraction* ξ_i , defined as

$$\xi_i \equiv \frac{f_i}{\sum_{j=1}^n f_j}. \quad (79)$$

The advantage is that, while $\ln(f_i/f_1)$ varies between $-\infty$ and $+\infty$ as we go from pure 1 to pure i , ξ_i varies between 0 and 1. Clearly,

$$\beta\mu_1 N = -\ln \left(\beta P \int dV \exp(-\beta PV) \frac{(Vq_1)^N}{N!} \sum_{\text{identities}} \prod_{i=1}^n \left(\frac{\xi_i}{\xi_1} \right)^{N_i} \int d\mathbf{s}^N \exp(-\beta U(\mathbf{s}^N)) \right). \quad (80)$$

How does μ_1 , the chemical potential of the reference species, change with the fugacity fractions of the other species? To see this we consider the derivative of eq. 80 with respect to ξ_i :

$$\left(\frac{\partial \beta\mu_1 N}{\partial \xi_i} \right)_{N, P, T, \{x_i | j \neq i\}} = - \left\langle \frac{N_i}{\xi_i} + \frac{N - N_1}{\xi_1} \right\rangle, \quad (81)$$

where we have used the fact that $d\xi_1 = -\sum_{j \neq i} d\xi_j$. Eq. 81 tells us how we can measure μ_1 changes as we change the chemical potential difference between species 1 and the other species. Let us consider the application to phase coexistence in a binary mixture. In that case we only vary ξ_2 . First we measure the excess chemical potential in phase I consisting of pure 1 and in phase II consisting of pure species 2 (for instance by thermodynamic integration). Next we compute the change in μ_1 in phase I as we increase ξ_2 from 0 and the corresponding change in μ_1 in phase II as we lower ξ_2 from 1. The point where $\mu_1^{(I)}(\xi_2) = \mu_1^{(II)}(\xi_2)$ is the coexistence point, because at that point $f_1^{(I)} = f_1^{(II)}$ and $f_2^{(I)} = f_2^{(II)}$. Note that we have not specified the nature of phase I and II. They could be liquid, solid or liquid crystalline.

The only practical problem that remains is the Monte Carlo sampling of $-\langle N_i/\xi_i + (N - N_1)/\xi_1 \rangle$ (eq. 81). Note that the N_i are the dependent variables. The ξ_i are imposed during a given simulation. In addition to the usual particle moves and volume changes we must now also consider a move where a particle changes identity. To this end, we select one of the N particles at random and with equal probability assign it one of the n possible identities. The probability of accepting such a trial move is

$$P_{acc} = \text{Min} \left(1, \frac{\xi_{i'}}{\xi_i} \exp(-\beta \Delta U(\mathbf{s}^N)) \right), \quad (82)$$

where $\Delta U(\mathbf{s}^N)$ denotes the change in potential energy of the system if we change the identity of a randomly selected particle from i into i' .

I conclude this discussion of the semi-grand ensemble with three comments. First of all, SGCMC is very well suited to study phase equilibria in multicomponent systems that are

also in chemical equilibrium. The reason is that every chemical equilibrium simply imposes a relation between the fugacities of the reacting species. Hence, the only effect of a chemical equilibrium is that the number of *independent* fugacities is reduced by one. In practice, the method cannot be used to study *any* chemical equilibrium: the total number of molecules should be conserved in the reaction.

Secondly, the SGCMC scheme can be used to simulate phase equilibria in truly polydisperse systems, including polydisperse solids. And finally, it can be quite advantageous to combine the SGCMC method with the Gibbs ensemble method for mixtures. In that case the fugacity ratios in both simulation boxes are kept the same. In other words, we allow particles in either box to change identity while remaining in the same box. But in addition we allow trial moves where we attempt to move a particle of the reference species 1 from one box to the other. Now the selection of the particle to be swapped goes as follows: first select box I or box II with equal probability. Next, select any molecule of type 1 in the selected box and try to insert it in the other box. The acceptance probability of such a move is given by eq. 64 (I should point out that the implementation that I suggest here is slightly different from the one advocated in ref. [53] and closer to the approach of Stapleton et al. [54]). The natural choice for the reference species 1 is clearly that species that can be swapped most efficiently, e.g. the smallest molecule in the system.

5 Conclusions

In this paper I have explained why free energy simulations are necessary and why such calculations require special techniques. Free energy calculations are of particular importance in material science because of the great practical importance of phase equilibria (possibly in conjunction with chemical equilibria). But I hope that I have also conveyed to the reader an appreciation of the second reason why free energy calculations are interesting: namely the physical insight that they provide in the nature of quantities that are usually considered to be quite abstract such as the chemical potential. Understanding the ‘microscopic’ meaning of a statistical mechanical quantity is always the first step in the construction of any theoretical approximation to estimate this quantity. In this context, I hope that free energy calculations may not only give us more data about complex materials, but also help us to construct better theoretical descriptions.

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